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Ultrasonic Measurement of Carotid Intima–Media Thickness in a Group of Iranian with No Cardiovascular Risk Factors

Background/Objective: To obtaining reference values for intima-media thickness (IMT) of the carotid arteries in the Iranian subjects without any known atherosclerosis risk factors.

Patients and Methods: A total of 400 subjects (146 male and 254 female, mean age 36.3±14 years in men and 35.9±12 years in women), with normal body mass index and no history or evidence of cardiovascular or peripheral vascular disease, hypertension, diabetes, thyroid diseases or smoking were examined. IMT was measured on a longitudinal ultrasound image of the carotid artery. Mean thickness was evaluated for the right common carotid (RCCA), right internal carotid (RICA), left common carotid (LCCA) and left internal carotid (LICA).

Results: The mean value of carotid IMT was 0.38±0.11 in women and 0.41±0.13 in men. For different age groups, the lowest mean thickness was 0.305±0.045, seen in the RCCA among 20-29-year-old cases, and the highest was 0.645±0.125, seen in the LICA of cases over 60. The mean thickness was higher in men than in women, in all four locations (all p values< 0.02 Linear regression models for prediction of IMT by age, were separately done in different groups of anatomical location and gender, and all models' R^2 were higher than 0.5.

Conclusion: Mean IMT in RCCA, RICA, LCCA and LICA in both genders and different age decades was lower than many reports, which may be due to ethnic factors or different inclusion criteria. Reference values of carotid IMT increase significantly with age and IMT is higher in men than in women.

Keywords: ultrasonography, intima–media thickness, atherosclerosis

Introduction

Atherosclerosis is a chronic multifactorial disease process. Intermediate endpoints are needed to better define the disease course and disease response to interventions during the asymptomatic period. Various noninvasive markers of early arterial wall alteration, such as arterial wall thickening and stiffening, endothelial dysfunction and coronary artery calcification are currently available, of which altered intima–media thickness (IMT) is a predictor of cardiovascular prognosis.[1, 2]

The relatively recent advances in ultrasound scanning of the carotid arteries have provided opportunities to assess IMT of the carotid artery by B-mode ultrasonography using a relatively simple method.

This technique yields information on atherosclerotic wall changes that cannot be assessed by angiography or MRI. An increased thickness of carotid IMT determined by B-mode ultrasound has been shown to be directly associated with an increased risk of myocardial infarction and stroke in older adults with no revious history of cardiovascular disease.[3]

Also, it has been shown that measurements of IMT by quantitative B-mode ultrasound imaging are a valid, sensitive, and reliable noninvasive method for early diagnosis of atherosclerosis and morphologic alterations at the carotid artery

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wall.[4,5] Even in the absence of discrete plaques, the combined thickness of the arterial intima and media, the so-called IMT, can be measured with B-mode ultrasonography with an automated, computerized system of imag analysis.[6-8]

However, for exact interpretation of these measurements, reference values for IMT should be determined. The present study provides normal values for IMT of the carotid artery in an Iranian population of healthy subjects without any cardiovascular risk factors.

Patients and Methods

Our study group consisted of 400 healthy volunteers who came to university-affiliated hospitals for reasons other than physical illness. They had no history of cardiovascular or peripheral vascular disease, hypertension, diabetes, thyroid diseases or smoking, and all of them had a normal body mass index (BMI) (between 18.5–24.9). Informed consent was obtained from all patients. We studied them with carotid ultrasonography. IMT measurements of the right common carotid (RCCA), left common carotid (LCCA), right internal carotid (RICA) and left internal carotid (LICA) arteries were obtained with the use of a high-resolution ultrasound unit (Hitachi EUB 405, Japan) equipped with a 7.5 MHz B-mode transducer. The boundaries of different layers of the carotid artery wall were visualized with high-resolution B-mode ultrasonography.

Subjects were examined in the supine position and measurements were made of both the right and left carotid arteries in the following manner. For better outcomes, all cases were asked to rotate their heads laterally, while keeping their shoulders in the lowermost possible position. We examined longitudinal ultrasound images of the carotid artery.[9] On this image, both the near and far walls have a double-line pattern with two parallel echogenic lines separated by a small hypoechogenic stripe. The correct identification of ECA and ICA was made according to the Zwiebel protocol.[9] Measurements were done for the far wall. Our scales for IMT measurement were 0.1 mm.

We used SPSS version 11.5 for statistical analysis. We used the t-test and simple linear regression for statistical analysis. Statistical significance was considered at a value of $p<0.05$.

Results

A total of 400 cases, 254 female (63.5%) and 146 male (36.5%) were evaluated, and the mean age was 35.9±12.4 and 36.4±14.4 years for women and men, respectively. Most cases were between 30 to 39 years of age (n=152, 38%). Dr

The minimum measured IMT in RCCA, RICA, LCCA, and LICA was 0.2mm and the maximum was 0.9mm. Mean IMT for age is shown in Table 1. The mean IMT of RCCA, RICA, LCCA and LICA increased with age for both genders (Figures 1a and b) ($p<0.0001$). The greatest difference was seen between the fifth and sixth decades of life (Figures 1a and b). The mean increase in IMT of different arteries by decade in men and women is shown in Table 1b.

Mean IMT in RCCA and LCCA in our cases was 0.38±0.11 and 0.40±0.12, respectively ($p<0.0001$), and also mean IMT in RICA and LICA in these cases was 0.40±0.11 and 0.41±0.12, respectively ($p<0.0001$). We measured these levels for both males and females, and these differences were significant (Table 2); IMT was significantly lower in women than in men, and we found that IMT increases with age ($p<0.0001$). Mean IMT in CCA in men and women was 0.38±0.11 and 0.41±0.13, respectively.

Mean IMT of RCCA was significantly different from that of RICA and LCCA in both genders. Also, the mean IMT of LICA significantly differed from that of LCCA and RICA in both genders (Tables 3a and b).

To predict the diameter of RCCA, RICA, LCCA and LICA by age, in both men and women, we performed a linear regression test. The resultant formulas are shown in Table 4.

In order to assess the correlation between IMTs on each side (for example RICA and RCCA) and in the same areas on the right and left (for example LCCA and RCCA) we used Spearman correlation coefficient test in paired samples and found significant correlation between paired samples (Table 5).

Discussion

B-mode ultrasound is a safe and relatively low-cost technique for measuring IMT. The American Cardiovascular Society state that carotid ultrasound is a safe

Table 1a. Mean IMT for decades of age.

Age (years)	Artery	Number	Mean	Range	95% CI
20-29	RCCA	135	0.305±0.045	0.2-0.4	0.3 ±0.09
	RICA		0.315±0.045	0.2-0.4	0.32 ±0.09
	LCCA		0.308±0.059	0.2-0.4	0.31 ±0.12
	LICA		0.315±0.035	0.2-0.4	0.32 ± 0.07
30-39	RCCA	152	0.365±0.063	0.3-0.5	0.37 ± 0.13
	RICA		0.393±0.055	0.3-0.6	0.39 ± 0.11
	LCCA		0.389±0.066	0.3-0.6	0.39 ± 0.13
	LICA		0.402±0.065	0.3-0.6	0.4 ± 0.13
40-49	RCCA	61	0.419±0.084	0.3-0.7	0.42 ± 0.17
	RICA		0.442±0.095	0.3-0.7	0.44 ± 0.19
	LCCA		0.418±0.147	0.3-0.8	0.42 ± 0.29
	LICA		0.468±0.101	0.3-0.8	0.47 ± 0.20
50-59	RCCA	19	0.552±0.1	0.4-0.8	0.55 ± 0.2
	RICA		0.6±0.081	0.5-0.8	0.6 ± 0.16
	LCCA		0.605±0.132	0.4-0.9	0.6 ± 0.26
	LICA		0.636±0.125	0.5-0.9	0.64 ± 0.25
>60	RCCA	33	0.563±0.183	0.4-0.8	0.56 ± 0.37
	RICA		0.639±0.102	0.4-0.8	0.64 ± 0.2
	LCCA		0.578±0.192	0.4-0.9	0.58 ± 0.38
	LICA		0.645±0.125	0.4-0.9	0.65 ± 0.25

RCCA: right common carotid artery; RICA: right internal carotid artery; LCCA: left common carotid artery; LICA: left internal carotid artery; CI: Confidence Interval

Table 1b. Mean increase in IMT by decades of age for men and women.

	Men	Women
RCCA	0.0785±0.066	0.0694±0.024
RICA	0.0873±0.065	0.0759±0.045
LCCA	0.0792±0.104	0.0774±0.027
LICA	0.0825±0.099	0.0826±0.040

(RCCA: right common carotid artery, RICA: right internal carotid artery, LCCA: left common carotid arter, LICA: left internal carotid artery).

technique for detection of subclinical atherosclerosis, especially, in asymptomatic cases over 45 years of age that it can have a predictive role for risk assessment. Many studies have shown a close association between IMT of the carotid artery measured by high-resolution ultrasonography and presence of coronary artery disease or atherogenic risk factors.

However, reference values for the IMT in healthy subjects had not been established in our country. We determined the reference values of carotid IMT with respect to age and gender in subjects with no history of atherosclerotic risk factors using ultrasound examination.

One major finding of the present study is that the IMT of carotid arteries was significantly higher in men than in women ($p < 0.012$) which are in agreement with many other reports.[10-13] Also, we found that carotid IMT increases significantly with age ($p < 0.0001$), as supported by other studies.[10-13]

In our study, IMT in RICA and LICA were higher than in RCCA and LCCA. We do not know the exact reason for the higher mean IMT of ICA in comparison to CCA, but we assume that this difference may be attributed to the bifurcation of the CCA and the

Table 2. Mean IMT in Iranian women and men.

Artery	Gender	Number	Mean	Minimum	95%CI	p value
RCCA	F	254	0.371±0.0987	0.2-0.8	0.371±0.19	0.01
	M	146	0.403±0.1254	0.2-0.8	0.403±0.25	
RICA	F	254	0.394±0.1063	0.2-0.8	0.394±0.20	0.02
	M	146	0.421±0.1259	0.2-0.8	0.421±0.24	
LCCA	F	254	0.389±0.1139	0.2-0.9	0.389±0.22	0.02
	M	146	0.420±0.1332	0.2-0.9	0.420±0.26	
LICA	F	254	0.403±0.1202	0.2-0.9	0.403±0.24	0.02
	M	146	0.433±0.1355	0.2-0.9	0.433±0.26	

Table 3a. Comparisons of mean IMT in different sites in women.

		Mean±SD	p value
Pair 1	RCCA	0.37±0.10	<0.0001
	RICA	0.39±0.11	
Pair 2	LCCA	0.39±0.11	<0.0001
	LICA	0.40±0.12	
Pair 3	RCCA	0.37±0.10	<0.0001
	LCCA	0.39±0.11	
Pair 4	RICA	0.39±0.11	0.005
	LICA	0.40±0.12	

RCCA: right common carotid artery, RICA: right internal carotid artery, LCCA: left common carotid artery, LICA: left internal carotid artery.

Table 3b. Comparisons of mean IMT in different sites in men.

		Mean±SD	p value
Pair 1	RCCA	0.40±0.12	<0.0001
	RICA	0.42±0.13	
Pair 2	LCCA	0.42±0.13	<0.0001
	LICA	0.43±0.13	
Pair 3	RCCA	0.40±0.12	<0.0001
	LCCA	0.42±0.13	
Pair 4	RICA	0.42±0.13	0.001
	LICA	0.43±0.13	

RCCA: right common carotid artery, RICA: right internal carotid artery, LCCA: left common carotid artery, LICA: left internal carotid artery.

entrance of more blood into the thinner artery; thus, we can conclude that IMT measured in the ICA should be higher than that of in the CCA.

Moreover, the IMT in LICA and LCCA is slightly more than in RICA and RCCA, which may be due to anatomical differences between the right and left carotid arteries and direct origination of the left carotid from the aorta.

Many studies have been performed on IMT in normal individuals as well as in atherosclerotic cases. These studies have IMT measured in the distal CCA in multiple age and gender subgroups. However, to the best of our knowledge, RCCA, RICA, LCCA and LICA were not examined individually.

Mean IMT in the Depairon study was 0.573±0.07 in men and 0.556±0.057 in women; in the Ando study was 0.61±0.15 in men and 0.58±0.14 in women; in the Gariepy study it was 0.56±0.12 in men and 0.51±0.06 in women; in the Allan study it was 0.91 in men and 0.84 in women.(10,11,13,14) All these means are statistically higher than in our study (0.42±0.133 and 0.389±0.113 in LCCA in men and women, respectively; all p values <0.001) This may be due to ethnic factors, but some other points should be considered. As was shown in our study (that reproduced results of other studies), IMT increases with age.[13,14] The mean age of our cases was under 40 years, which is lower than in some reports and may be the reason for the lower IMT in comparison to other studies.[12] Also, some authors believe that the presence of cardiovascular risk factors and diseases cause an increase in IMT in comparison to healthy persons without risk factors.[14] Some of the mentioned studies were done on cases with cardiovascular risk factors, which could have caused higher IMTs in those studies as compared to our study.[10, 11, 14]

We found a high correlation between IMTs in RCC and RIC, which means changes in IMTs of both occurs concommitently, which can be physiologically justified.

Linear regression tests, give formulas to predict diameters of the above arteries for each age group.

Table 4. Formulas for prediction of IMT.

Artery	Men		Women	
	Model	R^2	Model	R^2
RCCA	0.0074×(age)+0.134	0.707	0.0064×(age)+0.142	0.596
RICA	0.0074×(age)+0.146	0.741	0.0067×(age)+0.145	0.661
LCCA	0.0078×(age)+0.144	0.637	0.0078×(age)+0.120	0.610
LICA	0.0078×(age)+0.148	0.678	0.0079×(age)+0.120	0.640

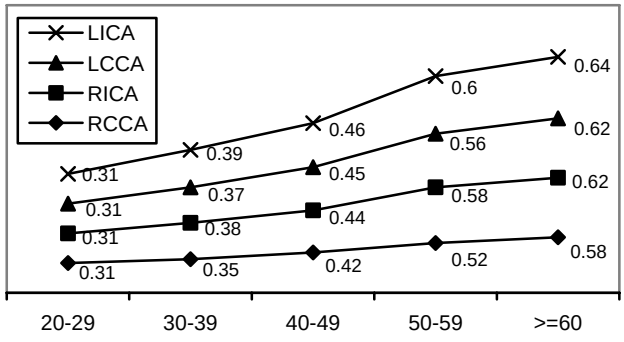
RCCA: right common carotid artery, RICA: right internal carotid artery, LCCA: left common carotid artery, LICA: left internal carotid artery.

Table 5. Correlation between Paired samples.

	Number	Correlation	p value
Paired1(RCCA,RICA)	400	0.904	0.0001
Paired2 (LCCA,LICA)	400	0.909	0.0001
Paired3(RCCA,LCCA)	400	0.853	0.0001
Paired4 (RICA,LICA)	400	0.838	0.0001

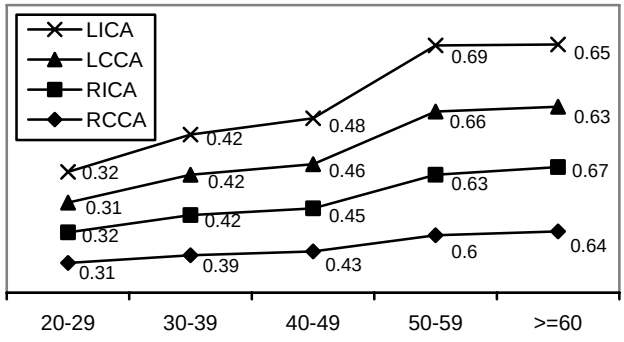
RCCA: right common carotid artery, RICA: right internal carotid artery, LCCA: left common carotid artery, LICA: left internal carotid artery.

Fig 1a. Mean of IMT in LICA, LCCA, RICA and RCCA in subsequent decades in women.



RCCA: Right Common Carotid Artery, RICA: Right Internal Carotid Artery, LCCA: Left Common Carotid Artery, LICA: Left Internal Carotid Artery.

Fig 1b. Mean of IMT in LICA, LCCA, RICA and RCCA in subsequent decades in men.



RCCA: Right Common Carotid Artery, RICA: Right Internal Carotid Artery, LCCA: Left Common Carotid Artery, LICA: Left Internal Carotid Artery.

Finally, further multicenter studies are required to investigate the refrence values for IMT in the normal population in our country.

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